FUNCTIONAL DEFICIENCY OF VITAMIN K IN HEMODIALYSIS PATIENTS

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OBJECTIVES

Functional deficiency of vitamin K (both vitamin K_1 and K_2), involved in the process of γ-carboxylation is postulated as one of the most relevant links between the chronic kidney disease and vascular calcification among hemodialysis patients.

AIM

The aim of this study was to determine the level of functional vitamin K deficiency and its relation to vitamin K_1 intake in HD patients.

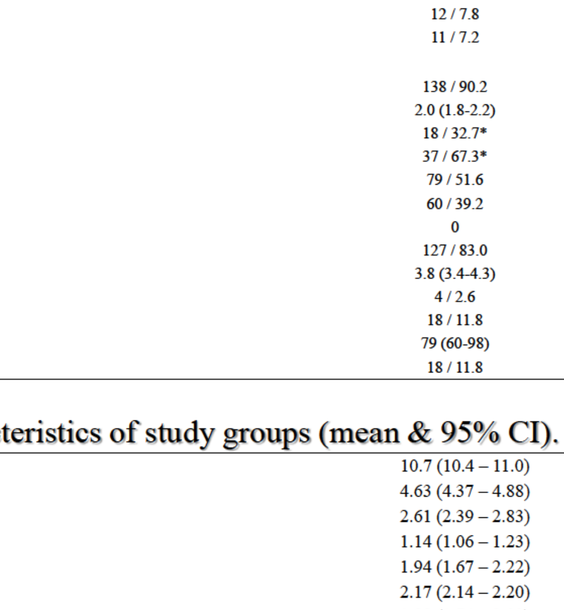
Table 1. Demographic and clinical characteristics of 153 hemodialysis patients (mean & 95% CI). *for patients with diabetes

Age *(years)*	62 (59 - 64)
Gender *(male/female)*	93/60
Body mass index *(kg/m²)*	25.5 (24.2-26.7)
Obesity (BMI≥30 kg/m²) (n/%)	27 / 17.6
Primary cause of CKD *(n/%)*	
Diabetes	43 / 28.1
Hypertension	17 / 11.1
Nephrolithiasis	8 / 5.2
Autosomal Dominant Polycystic Kidney Disease (ADPKD)	10/ 6.5
Ischemic nephropathy	3 / 2.0
Glomerulonephritis	24 / 15.7
Interstitial nephritis	13 / 8.5
Other or unknown	35 / 22.9
Time on dialysis *(months)*	48 (40-56)
Kt/V *(per HD session)*	1.21 (1.13-1.27)
Co-morbidity *(%)*	
Hypertension	138 / 90.2
Diabetes	55 / 35.9
Coronary artery disease	84 / 54.9
Stroke	12 / 7.8
Past kidney transplantation	11 / 7.2
Pharmacotherapy *(n/%)*	
Antihypertensive	138 / 90.2
No of antihypertensive drugs (n)	2.0 (1.8-2.2)
Oral anti-diabetic	18 / 32.7*
Insulin	37 / 67.3*
Antiplatelet	79 / 51.6
Statins	60 / 39.2
Fibrates	0
Oral phosphorous binders	127 / 83.0
Carbonate calcium dose (g/day)	3.8 (3.4-4.3)
Sevelamer hydrochloride	4 / 2.6
Cinacalcet	18 / 11.8
Cinaclcet dose (mg/day)	79 (60-98)
Alfacalcidol	18 / 11.8

Table 2. Biochemical characteristics of study groups (mean & 95% CI).

Hemoglobin *(g/dL)*	10.7 (10.4 – 11.0)
Total cholesterol *(mmol/L)*	4.63 (4.37 – 4.88)
LDL cholesterol *(mmol/L)*	2.61 (2.39 – 2.83)
HDL cholesterol *(mmol/L)*	1.14 (1.06 – 1.23)
Triglycerides *(mmol/L)*	1.94 (1.67 – 2.22)
Calcium *(mmol/L)*	2.17 (2.14 – 2.20)
Phosphorous *(mmol/L)*	1.88 (1.74 – 2.03)
Parathyroid hormone *(pg/mL)*	442 (318 – 618)
$25(OH)D_3$ *(ng/mL)*	22.9 (17.7 – 28.1)
ucMGP *(mg/mL)*	17.9 (16.3 – 19.5)
ucMGP > 9.2 mg/mL (%)	**77.1**
PIVKA II *(ng/mL)*	**0.59 (0.51 – 0.68)**
PIVKA II > 0.66 ng/mL *(%)*	**27.5**

Figure 1: The receiver operator curve analysis showing the threshold daily intake for vitamin K_1 resulting in increased plasma concentration of PIVKA II (>0.66 ng/mL).



METHODS

Protein induced vitamin K absence or antagonist-II (PIVKA-II) and uncarboxylated matrix Gla protein (ucMGP) were assessed by ELISA in 153 stable, prevalent HD patients and 20 apparently healthy adults (for PIVKA-II and ucMGP normal ranges establishment). Daily phylloquinone intake were assessed in addition to other macro- and micronutrients on the basis of food frequency questionnaire (FFQ).

RESULTS

Functional vitamin K deficiency defined as elevated PIVKA II levels was present in 27.5% of HD patients, and in 45% of cases was explained by insufficient phylloquinone intake for Polish population (> 55 µg for women and > 65 µg for men). Applying ROC analysis we showed that vitamin K_1 intake below 40.2 µg/day is associated with functional vitamin K deficiency. There was no correlation between plasma concentration of PIVKA II and ucMGP, that suggest that functional vitamin K deficiency does not influence ucMGP levels among HD patients. Plasma ucMGP concentrations were significantly greater in among HD patients than in healthy subjects (17.9 [16.3 - 19.5] vs. 7.1 [5.1 - 9.2] mg/mL; p<0.001).

Table 3. Macro- and micronutrients, and K_1 intake in 109 participants, who returned filled questionnaire (mean & 95% CI or *median with 25 and 75 percentiles).

	DHQ (N=109)	PIVKA II ≤0.66 ng/ml (N=75)	PIVKA II >0.66 ng/ml (N=34)	*Statistical significance*
Daily energy intake *(kcal/day)*	1639 (1461-1817)	1573 (1378-1768)	1675 (1289-2063)	Ns
Daily energy intake *(kcal/kg/day)*	23.2 (20.4-26.1)	22.1 (18.9-25.4)	23.1 (17.2-29.0)	Ns
Carbohydrates (g/day)	207 (184-229)	198 (175-221)	213 (163-263)	Ns
Proteins (g/day)	66 (58-73)	63 (51-82)	67 (51-82)	Ns
Proteins (g/kg/day)	0.92 (0.80-1.04)	0.87 (0.75-0.99)	0.94 (0.64-1.20)	Ns
Fat (g/day)	63 (55-71)	60 (51-70)	63 (47-80)	Ns
Fiber (g/1000 kcal)	9.3 (8.8-9.9)	9.3 (8.6-10.1)	9.4 (8.6-10.3)	Ns
Sodium *(g/day)*	2.92 (2.62-3.22)	2.78 (2.46-3.10)	3.06 (2.41-3.72)	Ns
Potassium *(mmol/day)*	62.9 (56.3-69.5)	60.8 (53.1-68.4)	63.6 (50.3-76.9)	Ns
Calcium *(mg/day)*	591 (519-663)	573 (493-653)	598 (439-742)	Ns
Magnesium (mg/day)	224 (202-248)	216 (192-240)	235 (183-286)	Ns
Phosphorus *(mg/day)*	963 (856-1070)	919 (800-1038)	988 (762-1213)	Ns
Phosphorus *(mg/kg/day)*	13.5 (11.7-15.4)	12.8 (10.8-14.9)	13.3 (9.5-17.1)	Ns
Vitamin K_1 *(µg/day)**	103 (43-221)	106 (56-224)	71 (37-203)	Ns
Vitamin K_1 intake <55 in men and <65 µg/day in women (%)	34	27	45	0.08

OBJECTIVES

1. Functional vitamin K deficiency in almost half of the population of haemodialysis patients is caused by low vitamin K_1 intake.
2. Uncarboxylated matrix Gla protein level seems not to be a surrogate of functional vitamin K_1 deficiency in haemodialysis patients.

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